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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,627	10/18/2004	Karsten Eulenberg	2923-657	8622

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ROTHWELL, FIGG, ERNST & MANBECK, P.C.
1425 K STREET, N.W.
SUITE 800
WASHINGTON, DC 20005

EXAMINER	
MITRA, RITA	
ART UNIT	**PAPER NUMBER**
1656	

NOTIFICATION DATE	DELIVERY MODE
01/16/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/511,627	EULENBERG ET AL.	
	Examiner	Art Unit	
	Rita Mitra	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *65-71* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *65-71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous office action has been withdrawn pursuant to 37 CFR 1.114. Applicants' submission filed on August 14, 2007 has been entered. The Geese Declaration under 37 CFR 1.132 (which is labeled "Draft") submitted on August 14, 2007 and August 28, 2007 is acknowledged.

Status of the Claims

Applicants' amendment in response to office action mailed March 14, 2007, filed on August 14, 2007 is acknowledged. Claims 1-64 have been cancelled. New claims 65-71 have been added. Therefore, claims 65-71 are currently under consideration.

Claims 65 in part, 66, 67, 68 in part, 69, 70 and 71 will be examined as they read on CG7956 polypeptide.

It should be also noted that the elected claims encompass i) the composition comprising CG7956 polypeptide not the CG7956 nucleic acids, and ii) the use of said polypeptide for the treatment of diseases, this is an intended use and not the method of treatment comprising administering CG7956 nucleic acid molecule or polypeptide encoded thereby to a patient as claimed in the newly added claims. Moreover new claims encompass gene therapy, which is a non-elected invention.

Therefore, claims 65 in part, 68 in part, 70 in part and 71 in part have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as they read on CG7956 nucleic acid and being drawn to a nonelected invention, there being no allowable generic or linking claim. Therefore, claims 65 in part, 66, 67, 68 in part, 69, 70 in part and 71 in part will be examined as far as they read on CG7956 polypeptide.

Response to Amendments and Remarks

Objection/ Rejection

Cancellation of claims 42 and 43 renders the objection moot.

Cancellation of claims 34, 42, 43, 51, 59, 60, 62 and 63 renders the rejection under 35 U.S.C. 112, first paragraph moot.

Cancellation of claims 34, 43 and 60 renders the rejection under 35 U.S.C. 112, second paragraph moot.

Cancellation of claims 34, 42, 51, 59, 62 and 63 renders the rejection under 35 U.S.C.103 moot.

New Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 65-71 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described

in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claimed invention is a method for the treatment of metabolic diseases, or dysfunctions, selected from the group consisting of obesity, diabetes, metabolic syndrome, eating disorder, cachexia, hypercholesterolemia, and dyslipidemia or to regulate triglyceride metabolism comprising administering of pharmaceutical composition comprising polypeptides set forth in SEQ ID NO: 14, SEQ ID NO: 15 and in Accession NO: ENSMUSP45910. However, there is no disclosure of any administration of these polypeptides to treat any diseases or regulate triglyceride metabolism.

The factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir., 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicted on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state

of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In the instant case no working examples are present for the method of treatment with this protein to treat said diseases. No *in vitro* or *in vivo* model has been presented. The specification does not provide any specific guidance on treating these conditions such as the patient population, dosage, regimen, routes of administration, the time and the treatment schedule as well as the effect of the proteins, nor most importantly is there any indication of the expected outcome of treatment. Since the specification fails to provide sufficient guidance on the treating conditions for these polypeptides, it is necessary to have additional guidance to carry out further experimentation to assess the effect of these polypeptides, which is used for the treatment, and to carry out further experimentation to assess the effect the polypeptide in the in vivo treatment. Without more guidance from the specification it would require undue and excessive experimentation for a person having skill in the art to be able to make and use the claimed method. Since the specification has not described the treating conditions for treating various disorders, nor has demonstrated the effect of polypeptide in treating or preventing various disorders, the invention is highly unpredictable regarding the outcome of the treatment.

When the factors are considered in their entirety, the Wands analysis dictates a finding of undue experimentation and thus, the claims are not enabled.

In the instant case no working examples are present with this protein to regulate triglyceride metabolism. No *in vitro* or *in vivo* model has been presented. The specification does not provide any specific guidance on conditions such as the patient population, dosage, regimen, routes of administration, the time and the treatment schedule as well as the effect of the proteins,

nor most importantly is there any indication of the expected outcome of treatment. Without more guidance from the specification it would require undue and excessive experimentation for a person having skill in the art to be able to make and use the claimed method. Since the specification has not described the treating conditions for regulating triglyceride metabolism the invention is highly unpredictable regarding the outcome of the treatment.

When the factors are considered in their entirety, the Wands analysis dictates a finding of undue experimentation and thus, the claims are not enabled.

In response to enablement rejection Applicants' arguments and remarks have been considered but they are not persuasive (pages 4-8 of the current 'Response'). It should be noted that Applicants are claiming a method of administration of a polypeptide of SEQ ID NO: 14 or SEQ ID NO: 15 or ENSMUSP45910 to a subject in need thereof in order to treat metabolic diseases or a method for regulating metabolism of triglycerides. However, the disclosure does not clearly explain the mechanism through which said polypeptides regulate triglyceride metabolism. To the examiner's understanding applicants have utilized insect models (i.e. drosophila) in order to demonstrate that mutation of the drosophila gene produces higher triglyceride content (Example 1, Fig. 1) in the chromosomal locus where the expression system has been integrated. However, said data is neither based on direct experiments performed on claimed polypeptides nor provides any information about the role of said polypeptides in regulation of triglyceride metabolism or in the treatment of metabolic disorders using these polypeptides. Applicants should note that the claims under examination are not a method of use of CG7956 gene but a method of use of its expression product.

Therefore, it is not clear how administration of the expression products of genes whose mutation can potentially result in triglyceride accumulation in insect cells can possibly regulate triglyceride metabolism in a subject in need thereof. Applicant is well aware that the influence of a gene's presence or absence in a disease is not necessarily carried over to its expression product due to post transcriptional events such as gene splicing phenomena etc. Even if, one assumes that claimed polypeptide had a measurable and positive impact on metabolic disorder regulation in subjects including and beyond insects, the following questions remain unanswered: (1) how much of said polypeptide should be administered, (2) what is the best route of administration and (3) how to assess the results short term and long term etc.

Therefore, due to lack of sufficient guidance and examples provided in the disclosure and due to unpredictability of prior art as how compositions comprising CG7956 polypeptides can impact triglyceride metabolism regulation in a subject one of skill in the art has to go through the burden of undue experimentation in order to practice the methods as claimed. Applicants are reminded that methods of use of polypeptides of claims 65-71 are subject to even more lack of enablement because it is unclear which regions (amino acids) within SEQ ID NOs: 14, 15 and ENSMUSP45910 (as explained above) should remain intact so that triglyceride metabolism regulation can be achieved in a subject in need thereof using the claimed polypeptide.

The "CG7956 Homolog in Vitro Validation" in the Geese Declaration has been considered, however the experiments described in the Declaration are not relevant to the instant claims. Claims require a method of treatment by administering a composition comprising recombinant polypeptides of SEQ ID NOs: 14, 15 and ENSMUSP45910SEQ encoded by CG7956 nucleic acid but declaration discloses *in vivo* experiments using the "knockout" genes.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 65, 66 and 67 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 65, 66 and 67 are indefinite because the claim lacks essential steps in the method of treating or preventing a metabolic disease/disorder. The omitted step is the outcome of the method. The term "treating metabolic disease" is not the end point of the method because it does not indicate the effect of the polypeptide administered, thus it is not clear whether the treatment is effective.

Conclusion

No claim is allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita Mitra whose telephone number is 571-272-0954. The examiner can normally be reached on M-F, 10:00 am-7:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Kathleen Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Rita Mitra, Ph.D.

November 10, 2007

/Jon P. Weber/
Jon P. Weber
Supervisory Patent Examiner, 1657